UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/351,778	07/12/1999	WILLIAM S. M. WOLD	16153-7775	1203

7590 04/17/2008

STEVEN L. HIGHLANDER
FULBRIGHT 7 JAWORSKI L.L.P.
600 CONGRESS AVENUE,
SUITE 2400
AUSTIN, TX 78701

EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
04/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte
WILLIAM S. M. WOLD, KAROLY TOTH, KONSTANTIN DORONIN,
and ANN E. TOLLEFSON

Appeal 2007-2573
Application 09/351,778
Technology Center 1600

Decided: April 17, 2008

Before DEMETRA J. MILLS, LORA M. GREEN, and
RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal[1] under 35 U.S.C. § 134 from the Examiner's final rejection of claims 11-15, 20-22, 24, 32-44, 60-75 and

---

[1] This Appeal was heard on March 11, 2008.

97-108.[2] We have jurisdiction under 35 U.S.C. § 6(b). Claims 13, 60, and 102 are representative of the claims on appeal, and read as follows:

13. A method for treating cancer in an animal having a tumor comprising administering to the tumor an adenovirus vector wherein said adenovirus vector is replication-competent in neoplastic cells and overexpresses an adenovirus death protein (ADP), wherein overexpression is defined as overexpression relative to *dl*309.

60. A method for treating cancer in an animal having a tumor, the method comprising administering to the tumor an adenovirus vector that is replication-competent in neoplastic cells and expresses an adenovirus death protein (ADP), wherein:

a) the ADP is expressed from an ADP coding sequence positioned under the control of a promoter other than the endogenous promoter for ADP;

b) the adenovirus vector comprises a deletion in the E3 region that removes a splice site for E3 mRNA;

c) the ADP is expressed from an ADP coding sequence flanked by a pre-mRNA splicing and cleavage/polyadenylation signal other then the pre-mRNA splicing and cleavage/polyadenylation signal normally associated with the ADP gene, and/or

d) the ADP is expressed from an ADP coding sequence that is positioned downstream of the coding sequence for another adenovirus mRNA, together with a sequence on the 5' side of the ADP coding sequence that allows for internal initiation of translation of ADP.

102. A method for treating cancer in an animal having a tumor, the method comprising administering to the tumor an adenovirus vector wherein said adenovirus vector is replication competent in neoplastic cells and overexpresses an adenovirus death protein (ADP), wherein overexpression is effected by one or more of the following modifications:

a) the ADP is expressed from an ADP coding sequence positioned under the control of a promoter other than the endogenous promoters for ADP;

---

[2] Claims 6-9, 16-19, 23, 25-31 and 76-84 have been withdrawn from consideration as being drawn to a non-elected invention, and claim 5 has been indicated as being allowable (Ans. 2). Claim 5 is drawn to "[a] recombinant adenovirus that comprises SEQ ID NO:1 or SEQ ID NO:2."

b) the adenovirus vector comprises a deletion in the E3 region that removes a splice site for an E3 mRNA;

c) the ADP is expressed from an ADP coding sequence flanked by a pre-mRNA splicing and cleavage/polyadenylation signal other than the pre-mRNA splicing and cleavage/polyadenylation signal normally associated with the ADP gene, and/or

d) the ADP is expressed from an ADP coding sequence that is positioned downstream of the coding sequence for another adenovirus mRNA, together with a sequence on the 5' side of the ADP coding sequence that allows for internal initiation of translation of ADP.

We reverse.

ISSUE

The Examiner contends that each of claims 11-13, 32-44, 60, 61, 68, 69, 72-75, 97-99, and 101-108 are anticipated under 35 U.S.C. § 102(e) by Henderson (US 6,197,293 B1, Mar. 6, 2001) or Little (US 6,254,862 B1, Jul. 3, 2001), and that each of claims 13, 20-22, 60, and 64-66 are rendered obvious under 35 U.S.C. § 103(a) over the combination of Henderson or Little as combined with Freytag (Freytag *et al*, "A Novel Three-Pronged Approach to Kill Cancer Cells Selectively: Concomitant Viral, Double Suicide Gene, and Radiotherapy," *Human Gene Therapy*, Vol. 9, pp. 1323-33 (1998)); and that the Declarations of the Inventors submitted under 37 C.F.R. § 1.131 are not sufficient to antedate the Henderson and Little references.

Appellants contend that Henderson and Little are not prior art under 35 U.S.C. § 102(e) as the Declarations submitted under 37 C.F.R. § 1.131 are sufficient to establish invention of the claimed subject matter prior to the effective filing dates of Henderson and Little.

Thus, the only issue to be decided on Appeal is: Are the Declarations of the Inventors submitted under 37 C.F.R. § 1.131 sufficient to antedate the Henderson and Little references?

FACTS

Claims 11-13, 32-44, 60, 61, 68, 69, 72-75, 97-99 and 101-108 stand rejected under 35 U.S.C. § 102(e) as being anticipated by either Henderson or Little. In addition, claims 13, 20-22, 60, and 64-66 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Henderson or Little as combined with Freytag.

In Appeal No. 2005-1444, decided January 26, 2006, a prior merits panel[3] affirmed the anticipation rejection over both Henderson and Little (Decision on Appeal, p. 13). The obviousness rejection based on both of those references was also affirmed (*id.* at 19). Moreover, the panel found that the Rule 131 declaration could not be relied on to overcome a reference that claims the same subject matter (*id.* at 16-18).

Appellants filed a Request for Rehearing on May 3, 2006, arguing that 2005-1444 merits panel failed to conduct a proper analysis to determine whether Henderson and Little claimed the same subject matter as the instant Application. (Request for Reh'g, p. 3.) The merits panel[4] that decided the rehearing agreed, and remanded the Application back to the technology center in order for the Examiner to determine "if the instant claims anticipate or render obvious claims of the Henderson/Little patents, and if claims of the

[3] The merits panel in Appeal No. 2005-1444 was Ellis, Adams, and Green.
[4] The merits panel on the Decision on Request for Rehearing was Adams, Mills, and Green.

Henderson/Little patents anticipate or render obvious the claims on appeal." (Decision on Request for Reh'g, p. 7.)

The Examiner, after consulting with an interference specialist in Tech Center 1600, determined that there is no potential interference between the pending claims of the instant application and the claims of either of the Henderson or Little patents (Supp. Ans.[5] 2).

Appellants had submitted two Declarations under 37 C.F.R. § 1.131 in order to demonstrate prior conception and diligence to reduction to practice of the claimed subject matter before the effective filing dates of the Henderson and Little patents (App. Br.[6] 16).

Appellants assert that Exhibit B of the first Declaration submitted under 37 C.F.R. § 1.131 (hereinafter "Wold I Declaration") is a research proposal which describes the goal of the inventors to prepare adenovirus vectors that overexpress the ADP gene (referred to as the E3-11.6K gene in Exhibit B), and their use as therapeutic agents to kill malignant cells in humans (App. Br. 17).

The Wold I Declaration, Appellants assert, demonstrates construction and testing of the KD1 vector, which is the same vector described in the Specification (*id.* at 18). The KD1 vector was constructed by removing the E3 genes, with reinsertion of the ADP gene (*id.*). Appellants argue that the Wold I Declaration, along with the second Declaration submitted under 37 C.F.R. § 1.131 (hereinafter "Wold II Declaration"), provides evidence of

---

[5] All references to the Supplemental Answer (Supp. Ans.) are to the Supplemental Examiner's Answer mailed November 2, 2006.

[6] All references to the Appeal Brief (App. Br.) are to the Appeal Brief dated November 18, 2004. Copies of the two Declarations submitted under 37 C.F.R. § 1.131 can be found in the Evidence Appendix of the Appeal Brief as attachments 4 and 5.

further studies with KD1, including successful testing in an animal model (*id.* at 19-20). Thus, Appellants conclude that the Declarations show conception plus diligence to a reduction of practice (*id.* at 20).

The Examiner asserts that Exhibit B of Wold I does not demonstrate that adenoviral vectors that overexpress ADP are a goal of the research proposal (Ex. Ans. 23). The Examiner also argues that the Exhibit does not demonstrate conception of a vector that is replication competent in neoplastic cells (*id.* at 24-25) as required by claims 13, 60, and 102. According the Examiner, the Exhibit in fact teaches away from the use of such vectors by stating that the therapeutic vectors should "probably be defective." (*Id.* at 25.) The Examiner agrees, however, that "the KD1 vector was conceived and made prior to the effective date of the Henderson and Little patents." (*Id.* at 26.)

In response, Appellants argue that the Examiner is only contesting the evidence of conception (Reply Br.[7] 11). As the Examiner concurs that KD1 vector was conceived before the effective date of the Henderson and Little patents, we agree that the issue is conception, particularly the conception of a "vector [that] is replication-competent in neoplastic cells and overexpresses an adenovirus death protein (ADP)" as recited in claim 13. We first focus our attention on Exhibit B of the Wold I Declaration.

Exhibit B, a research proposal, states that "[s]ince the 11.6K protein [ADP protein] can promote the death of adenovirus-infected cells, it has the potential use as a therapeutic agent to kill cells, e.g., malignant cells, in humans." (Exhibit B, p. 3.) The Exhibit goes on to state that there are "two

[7] All references to the Reply Brief (Reply Br.) are to the Reply Brief dated February 25, 2005).

general classes of adenovirus vectors, nondefective and defective for replication in cultured human cells." (*Id.* at 4.) The Exhibit notes that because the eventual hope is the design of an adenovirus vector to promote cell death, "it will be important to limit the infection *in vivo* to the target tissue, and to minimize infection of healthy tissue. Therefore, the vector should probably be defective. The expression of the 11.6K protein could be limited to the tumor by direct infection into the tumor, or by use of tissue-specific promoter to drive expression of the 11.6K gene." (*Id.* at 5.)

The Exhibit states:

> Our vector will have an Ad5 backbone, and it will be deleted in the E1A, E1B, and E3 regions. The 11.6K gene will be inserted into an expression cassette wherein transcription will be driven by the cytomegalovirus immediate early promoter, and the pre-mRNA will be processed using SV40 polyadenylation and splicing signals. The expression cassette will be inserted into the E1A/E1B region . . ., and plaques will be picked on 293 cells. Plaques of vector expressing 11.6K should be larger (more cell lysis and virus spread) than plaques from vector lacking 11.6K. Plaques will be expanded into virus stocks, and high-level expression of the 11.6K protein will be confirmed.

(*Id.* at 6.)

As to future experiments, the Exhibit notes that optimization of 11.6K expression will be attempted, whether the E3 region should be included will be explored, as will whether the use of a nondefective vector will be useful (*id.* at 8).

Also as to levels of expression of ADP, Exhibits A11, A12 and A14 of the Wold I Declaration use the annotations of "ADP+++," "ADP++,"

"WT," and "ADP-," thus providing evidence that the inventors were aware of and studying adenovirus vectors that express different levels of ADP.

PRINCIPLES OF LAW

37 C.F.R. § 1.131 states, in relevant part:

> (a) When any claim of an application or a patent under reexamination is rejected, the inventor of the subject matter of the rejected claim, the owner of the patent under reexamination, or the party qualified under §§ 1.42, 1.43, or 1.47, may submit an appropriate oath or declaration to establish invention of the subject matter of the rejected claim prior to the effective date of the reference or activity on which the rejection is based.
> . . . .
> b) The showing of facts shall be such, in character and weight, as to establish reduction to practice prior to the effective date of the reference, or conception of the invention prior to the effective date of the reference coupled with due diligence from prior to said date to a subsequent reduction to practice or to the filing of the application. Original exhibits of drawings or records, or photocopies thereof, must accompany and form part of the affidavit or declaration or their absence must be satisfactorily explained.

Thus, a declaration under 37 C.F.R. § 1.131 must establish possession of either the whole invention claimed or of something falling within the claim such as a species of a claimed genus, such that the claim as a whole reads on it. *See In re Tanczyn*, 347 F.2d 830, 831-32 (CCPA 1965); *see also* MPEP § 715.02 (8th ed., as revised September 2007). Moreover, where the disclosure in the prior art is only a single species of a genus claim, appellant can overcome the rejection through the use of a Rule 131 declaration by showing prior possession of the species disclosed in the reference. *In re Stempel*, 241 F.2d 755, 759, (CCPA 1957).

ANALYSIS

We find that the two Wold Declarations submitted under 37 C.F.R. § 1.131 are sufficient to establish invention of the claimed subject matter prior to the effective date of the Henderson and Little patents.

The Examiner does not dispute that Appellants had possession of the KD1 adenovirus vector prior to the effective filing dates of the Henderson and Little patents (Supp. Ans. 5). The position of the Examiner is, relying on *Invitrogen Corp. v. Clontech Laboratories, Inc.*, 429 F.3d 1052 (Fed. Cir. 2005), that

> it was not until several months after the effective filing date of the Henderson and Little patents, that it was known or appreciated that KD1 overexpressed ADP (Wold I, ¶¶ 7 & 8), and later still that KD1 had been considered as potentially being useful for treating cancer (Wold II, ¶¶ 4 & 5).
>
> Consequently as per the ruling in *Invitrogen*, it was not until the effective date of the Henderson and Little patents that a method of treating cancer with KD1 was conceived by Appellant[s].

(Supp. Ans. 5.)

The *Invitrogen* case involved an appeal of a partial summary judgment invalidating claims in three related patents as being anticipated by prior art under § 102(g)(2). *Invitrogen*, 429 F.3d at 1057. The party challenging the validity of the patents was required "to identify clear and convincing evidence of the factual underpinnings for . . . conception." *Id.* at 1063. Moreover, all reasonable factual inferences had to be made in favor to Invitrogen, the patentee. *Id.*

The invention in question was drawn to a genetically engineered reverse transcriptase with no RNase H. *Id.* at 1062. The issue in *Invitrogen*

was whether it was appreciated in the prior art applied under § 102(g)(2) that the engineered reverse transcriptase retained DNA polymerase activity but was RNase H minus, *see id.* at 1063-64, that is whether Clontech, the party challenging the patents, established by clear and convincing evidence that it was recognized in the prior art applied under § 102(g)(2) that the engineered reverse transcriptase retained DNA polymerase activity but were RNase H minus, *see id.* at 1066.

That is not the issue before us in the instant appeal. The issue here is: Have the Declarations filed under 37 C.F.R. § 1.131 established by a preponderance of the evidence that Appellants conceived the instant invention, coupled with due diligence from prior to said date to a subsequent reduction to practice or to the filing of the application, prior to the effective filing date of the Henderson and Little patent?

First, as set forth in *Stempel*, Appellants need only show prior possession of a species of the invention disclosed in the reference. In affirming the anticipation rejections over Henderson and Little, it was acknowledged that Henderson and Little did not acknowledge any level of overexpression of ADP in the adenovirus vectors taught by those references. (Decision on Appeal, p. 13.) The prior merits panel found that claim 13 "recites that the 'adenovirus vector. . . overexpresses an adenovirus death protein, wherein overexpression is defined as overexpression relative to d1309.' The claim does not require any particular level of overexpression, thus all that is required by claim 13 is *any* measurable level of ADP expression over that of *dl*309." (Decision on Appeal, p. 14-15.)

Moreover, the rejection was affirmed on the basis that there was "enough evidence on the record demonstrating that such a level of

overexpression would be inherent in the recombinant adenoviruses expressing ADP taught by Henderson and Little." (*Id.*) As found by the prior merits panel,

> Appellants prepare the adenoviruses required by the method of claim 13 by deleting the E3 region, and inserting the ADP gene from Ad5. *See* Specification, Example 1, page 20-21. Similarly, Henderson and Little also deleted the E3 region, and then inserted the ADP gene from Ad2. *See* Henderson, Col. 48, Example 6, lines 15-33; Little, Col. 38, Example 5, lines 20-25. As the adenoviruses taught by the Henderson and Little - and those taught by the instant specification were constructed in an analogous manner, *i.e.*,deletion of the E3 region followed by introduction of an ADP coding region, absent evidence to the contrary, one of ordinary skill in the art would expect the recombinant adenoviruses of Henderson and Little to express comparable amounts of ADP as the recombinant adenoviruses taught by the instant specification.

(*Id.* at 14-15.)

As the Examiner agrees that "the KD1 vector was conceived and made prior to the effective date of the Henderson and Little patents" (Answer at 26), Appellants have shown prior possession of the species disclosed by the reference.

Second, it is clear from the attachments to the Wold I Declaration that an adenovirus that expressed increased levels of ADP was a goal. As noted in Exhibit B of Wold I Declaration, it was recognized that ADP was necessary for cell death. The Exhibit also noted that optimization of 11.6K expression would be attempted (Exhibit B at 8). That, along with Exhibits A11, A12 and A14 of the Wold I Declaration, which use the annotations of "ADP+++," "ADP++," "WT," and "ADP-," demonstrate that increased

expression of ADP was a goal. Thus, there is evidence that the inventors had conceived of "overexpression" of ADP as required by the claims.

Third, Exhibit B is evidence that the use of adenoviral vectors for the killing of malignant cells in humans (Exhibit B 3) , *i.e.*, that the vectors may be useful in the treatment of cancer. Moreover, the Exhibit contemplates the use of both replication competent and replication defective vectors, and also contemplates the use of adenoviral vectors that have promoters that are tissue specific (Exhibit B 5-6 and 8). The fact that the replication defective vectors were also contemplated does not negate the fact that the Exhibit also contemplated, and thus conceived of the use of vectors that were replication-competent.

CONCLUSION

In summary, we find that the Declarations of the Inventors submitted under 37 C.F.R. § 1.131 are sufficient to antedate the Henderson and Little references, and thus those references are not available as prior art. We thus reverse the rejection of claims 11-13, 32-44, 60, 61, 68, 69, 72-75, 97-99 and 101-108 under 35 U.S.C. § 102(e) as being anticipated by either Henderson or Little, as well as the rejection of claims 13, 20-22, 60, and 64-66 under 35 U.S.C. § 103(a) as being obvious over the combination of Henderson or Little as combined with Freytag.

REVERSED

Ssc:

STEVEN L. HIGHLANDER
FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVENUE, SUITE 2400
AUSTIN, TX 78701